

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of: **Garvey et al**

Application No: **09/478,222**

Group Art Unit: **1627**

Filed: **January 5, 2000**

Examiner: **B. Celsa**

Nitrosated and Nitrosylated Alpha-Adrenergic Receptor Antagonists, Compositions and Methods of Use

Attorney Docket No: **102258.346**

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Assistant Commissioner of Patents
Washington, DC 20231

PETITION FROM REQUIREMENT FOR RESTRICTION UNDER 37 C.F.R. § 1.144

Applicants Petition under 37 C.F.R. § 1.144 from the Examiner's Restriction

Requirement dated March 22, 2001, which was made final in the Office Action dated June 29, 2001. Applicants respectfully request that this Petition be forwarded to the Group Director for timely consideration

I. The Restriction Requirement

On March 22, 2001, the Examiner made a seven-way restriction requirement to claims 35-69.

On April 13, 2001, Applicants traversed the Examiner's seven-way restriction requirement and provisionally elected Examiner's Group VI drawn to compositions comprising S-nitrosothiol compounds.

In the office action dated June 29, 2001, the examiner maintained his seven-way restriction requirement and then made the restriction requirement final.

This Petition is timely filed: Applicants requested reconsideration under 37 C. F. R. § 1.143 and made a provisional election with traverse. The Examiner then made the restriction requirement final.

Petition from Requirement for Restriction under 37 C.F.R. § 1.144
Application No. 09/478,222

II The Pending Claims are Related

Applicants pending claims 35-69 with respect to the restriction requirement are outlined below. All the claims are directed to **NO donating compounds**. The pending claims are attached hereto as Appendix 1.

Group I	Claims 35-42	Compositions comprising NO donating compounds containing compounds (nucleotides, proteins) for the treatment of human impotence
Group II	Claims 43-47	Compositions comprising NO donating compounds that induce endogenous NO production for the treatment of human impotence
Group III	Claims 48-52	Compositions comprising NO donating compounds such as 2-hydroxy-2-nitrosohydrazine for the treatment of human impotence
Group IV	Claims 53-56	Compositions comprising NO donating compounds such as (E)-alkyl-2-((E)-hydroximino)-5-nitro-3-hexene amine/amide for the treatment of human impotence
Group V	Claims 57-60	Compositions comprising NO donating compounds such as sydnonimine compounds for the treatment of human impotence
Group VI	Claims 61-65	Compositions comprising NO donating compounds such as S-nitrosothiol compounds for the treatment of female impotence
Group VII	Claims 66-69	Compositions comprising NO donating compounds such as NONOate compounds for the treatment of human impotence

III. Restriction is Not Proper When the Claims are Related

As stated in MPEP §808.02, “[w]here, as disclosed in the application, the several inventions claimed are related, and such related inventions are not patentably distinct as claimed, restriction under 35 U. S. C. §121 is never proper (MPEP §806.05).”

Petition from Requirement for Restriction under 37 C.F.R. § 1.144
Application No. 09/478,222

All the pending claims are related and directed to method of treating human or female impotence by administration of a **nitric oxide donating compound**. Thus, the restriction requirement is not proper. To show that the inventions are distinct, the Examiner must show either that (1) there is a separate classification of the claims; (2) a separate status in the art when they are classifiable together; or (3) a different field of search.

None of these three criteria have been shown with the claims of this application:

Applicants respectfully submit that the Examiner's refusal to consider claims 35-69 together in the pending application is improper, and these claims should be appropriately grouped and searched together. Further, it will not place an undue burden on the Examiner to conduct the search that is directed to claims 35-69 together.

IV. Related Applications

Examiner Celsa examined and allowed grandparent application, U. S. Serial No. 08/714,313, issued as U. S. Patent 5,994,294, a copy of which is attached hereto as Appendix 2. In this patent Examiner Celsa allowed claims that included the nitrosated/nitrosylated compound of Formula II in combination with all nitric oxide donors (i.e., a compound donates, transfers or releases nitrogen monoxide, induces the production of endogenous endothelium-derived relaxing factor, stimulates endogenous synthesis of nitrogen monoxide or is a substrate for nitric oxide synthase). In the present application, the claims are directed to the nitric oxide donor compounds alone (i.e. without the nitrosated/nitrosylated compound of Formula II). The specification describing these nitric oxide donor compounds is the same in both applications, and the claims for the nitric oxide donor compounds in the grandparent application were not restricted to Groups I to VII.

Examiner Celsa examined and allowed great grandparent application, U. S. Serial No. 08/595,538, issued as U. S. Patent 5,932,538, a copy of which is attached hereto as Appendix 3. In this patent Examiner Celsa allowed claims that included the nitrosated/nitrosylated compound of Formula III in combination with all nitric oxide donors (i.e., a compound donates, transfers or releases nitrogen monoxide, induces the production of endogenous endothelium-derived relaxing factor, stimulates endogenous synthesis of nitrogen monoxide or is a substrate for nitric oxide synthase). In the present application, the claims are directed to the nitric oxide donor compounds alone (i.e. without the nitrosated/nitrosylated compound of Formula III). There was no

Petition from Requirement for Restriction under 37 C.F.R. § 1.144
Application No. 09/478,222

restriction requirement in the great grandparent application with respect to the nitric oxide donors.

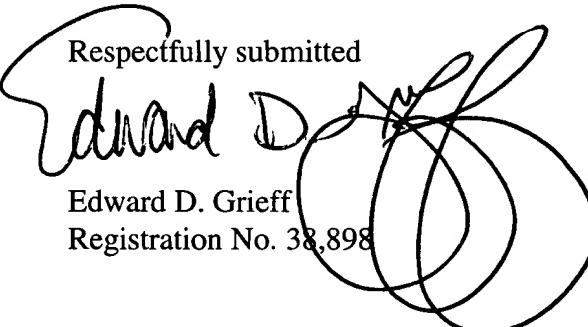
Other allowed U.S. patents that contain claims for nitric oxide donor compounds are U. S. Patent Nos. 5,874,437, 5,958,926, 6,043,233, 6,048,858, 6,057,347, 6,083,515, 6,133,272, 6,172,060, 6,172,068, 6,177,428, 6,197,778, and 6,197,782. Again, there was no restriction requirement in any of these application with respect to the nitric oxide donor compounds.

Additionally, pending patent application, U. S. Serial No. 09/354,424, has claims directed to the treatment of sexual dysfunctions by administration of nitric oxide donating compounds. Again, there was no restriction requirement in this application with respect to the nitric oxide donating compounds.

In view of the fact that numerous applications have been examined and allowed with the NO donor compounds, and that no election of species or restriction requirement was issued for the individual NO donor compounds in any of these other applications, Applicants respectfully submit that the election of species and restriction requirement in the present application is improper and respectfully request that it be withdrawn.

V. Conclusion

Applicants respectfully request that the restriction requirement be withdrawn, and that claims 35-69 be examiner together in the present application.

Respectfully submitted

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of: **GARVEY et al**

Application No: **09/478,222**

Group Art Unit: **1627**

Date Filed: **January 5, 2000**

Examiner: **B. Celsa**

Title: **NITROSATED AND NITROSYLATED ALPHA-ADRENERGIC RECEPTOR ANTAGONIST COMPOUNDS, COMPOSITIONS AND THEIR USES**

Attorney Docket No: **102258.346**

Assistant Commissioner of Patents
Washington, DC 20231

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Pending Claims

35. A method for treating human impotence in a individual in need thereof comprising administering to the individual a therapeutically effective amount of a composition comprising a compound that donates, transfers or releases nitrogen monoxide and a pharmaceutically acceptable carrier,

wherein the compound that donates, transfers or releases nitrogen monoxide is:

- (i) a compound comprising at least one ON-N- or ON-C- group,;
- (ii) a nitrite comprising at least one -O-NO group;
- (iii) a compound comprising at least one O₂N-O-, O₂N-N-, O₂N-S- or O₂N-C- group;
- (iv) a compound of the formula (R)_u-A-M-(NO)_v, wherein R is a polypeptide, an amino acid, a sugar, an oligonucleotide, a straight or branched, substituted or unsubstituted, aromatic or aliphatic hydrocarbon or a heterocyclic group; A is sulfur, oxygen or nitrogen; u and v are each independently integers of 1, 2 or 3; and M is a metal; or
- (v) a N-oxo-N-nitrosamine of the formula R₁R₂-N(O-M⁺)-NO, wherein R₁ and R₂ are each independently a polypeptide, an amino acid, a sugar, an oligonucleotide, a straight or branched, substituted or unsubstituted, aromatic or aliphatic hydrocarbon or a heterocyclic group; and M⁺ is a metal cation.

36. The method of claim 35, wherein the nitrite comprising at least one -O-NO group is an ON-O-protein, an ON-O-polypeptide, an ON-O-amino acid, an ON-O-carbohydrate, a straight or branched, saturated or unsaturated ON-O-alkyl compound, a straight or branched, saturated or unsaturated ON-O-aryl compound or a straight or branched, saturated or unsaturated ON-O-heterocyclic compound.

37. The method of claim 35, wherein the compound comprising at least one ON-N- or ON-C- group is an ON-N-polypeptide, an ON-C-polypeptide, an ON-N-amino acid, an ON-C-amino acid, an ON-N-sugar, an ON-C-sugar, an ON-N-oligonucleotide, an ON-C-oligonucleotide, a straight or branched, saturated or unsaturated, substituted or unsubstituted ON-N-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted ON-C-hydrocarbon, an ON-N-heterocyclic compound or an ON-C-heterocyclic compound.

38. The method of claim 35, wherein the compound comprising at least one O₂N-O-, O₂N-N-, O₂N-S- or O₂N-C- group is an O₂N-O-polypeptide, an O₂N-N-polypeptide, an O₂N-S-polypeptide, an O₂N-C-polypeptide, an O₂N-O-amino acid, an O₂N-N-amino acid, an O₂N-S-amino acid, an O₂N-C-amino acid, an O₂N-O-sugar, an O₂N-N-sugar, an O₂N-S-sugar, an O₂N-C-sugar, an O₂N-O-oligonucleotide, an O₂N-N-oligonucleotide, an O₂N-S-oligonucleotide, an O₂N-C-oligonucleotide, a straight or branched, substituted or unsubstituted, aromatic or aliphatic O₂N-O-hydrocarbon, a straight or branched, substituted or unsubstituted, aromatic or aliphatic O₂N-N-hydrocarbon, a straight or branched, substituted or unsubstituted, aromatic or aliphatic O₂N-S-hydrocarbon, a straight or branched, substituted or unsubstituted, aromatic or aliphatic O₂N-C-hydrocarbon, an O₂N-O-heterocyclic compound, an O₂N-N-heterocyclic compound, an O₂N-S-heterocyclic compound, or an O₂N-C-heterocyclic compound.

39. The method of claim 38, wherein the compound comprising at least one O₂N-O-, O₂N-N-, O₂N-S- or O₂N-C- group is an O₂N-S-polypeptide, an O₂N-S-amino acid, an O₂N-S-sugar, an O₂N-S-oligonucleotide, a straight or branched, substituted or unsubstituted, aromatic or aliphatic O₂N-S-hydrocarbon, or an O₂N-S-heterocyclic compound.

40. The method of claim 35, wherein the human impotence is male impotence.

41. The method of claim 35, wherein the human impotence is female impotence.

42. The method of claim 35, wherein the compound that donates, transfers or releases nitrogen monoxide is administered topically.

43. A method for treating human impotence in an individual in need thereof comprising administering to the individual a therapeutically effective amount of a composition comprising a compound that induces the production of endogenous endothelium-derived relaxing factor, stimulates endogenous synthesis of nitrogen monoxide, or is a substrate for nitric oxide synthase and a pharmaceutically acceptable carrier.

44. The method of claim 43, wherein the compound that induces the production of endogenous endothelium-derived relaxing factor, stimulates endogenous synthesis of nitrogen monoxide, or is a substrate for nitric oxide synthase is L-arginine.

45. The method of claim 43, wherein the human impotence is male impotence.

46. The method of claim 43, wherein the human impotence is female impotence.

47. The method of claim 43, wherein the compound that induces the production of endogenous endothelium-derived relaxing factor, stimulates endogenous synthesis of nitrogen monoxide, or is a substrate for nitric oxide synthase is administered topically.

48. A method for treating human impotence in an individual in need thereof comprising administering to the individual a therapeutically effective amount of a composition comprising a 2-hydroxy-2-nitrosohydrazine compound and a pharmaceutically acceptable carrier.

49. The method of claim 48, wherein the 2-hydroxy-2-nitrosohydrazine

50. The method of claim 48, wherein the human impotence is male impotence.

51. The method of claim 48, wherein the human impotence is female impotence.

52. The method of claim 48, wherein the composition is administered topically.

53. A method for treating human impotence in an individual in need thereof comprising administering to the individual a therapeutically effective amount of a composition comprising at least one of an (E)-alkyl-2-((E)-hydroxyimino)-5-nitro-3-hexene amine and an (E)-alkyl-2-((E)-hydroxyimino)-5-nitro-3-hexene amide, and a pharmaceutically acceptable carrier.

Pending Claims
US Application No. 09/478,222

54. The method of claim 53, wherein the human impotence is male impotence.
55. The method of claim 53, wherein the human impotence is female impotence.
56. The method of claim 53, wherein the composition is administered topically.
57. A method for treating human impotence in an individual in need thereof comprising administering to the individual a therapeutically effective amount of a composition comprising a sydnonimine compound and a pharmaceutically acceptable carrier.
58. The method of claim 57, wherein the human impotence is male impotence.
59. The method of claim 57, wherein the human impotence is female impotence.
60. The method of claim 57, wherein the composition is administered topically.
61. A method for treating female impotence in a female individual in need thereof comprising administering to the female individual a therapeutically effective amount of a composition comprising an S-nitrosothiol compound and a pharmaceutically acceptable carrier.
62. The method of claim 61, wherein the composition is administered topically.
63. The method of claim 61, wherein the S-nitrosothiol compound is S-nitroso-N-acetylcysteine, S-nitroso-captopril, S-nitroso-homocysteine, S-nitroso-cysteine or S-nitroso-glutathione.
64. The method of claim 63, wherein the S-nitrosothiol compound is S-nitroso-glutathione.
65. The method of claim 61, wherein the S-nitrosothiol compound is
 - (i) $\text{CH}_3(\text{C}(\text{R}_e)(\text{R}_f))_x\text{SNO}$;
 - (ii) $\text{HS}(\text{C}(\text{R}_e)(\text{R}_f))_x\text{SNO}$;
 - (iii) $\text{ONS}(\text{C}(\text{R}_e)(\text{R}_f))_x\text{B}$; or
 - (iv) $\text{H}_2\text{N}-\text{CH}(\text{CO}_2\text{H})-(\text{CH}_2)_x-\text{C}(\text{O})\text{NH}-\text{CH}(\text{CH}_2\text{SNO})-\text{C}(\text{O})\text{NH}-\text{CH}_2-\text{CO}_2\text{H}$;

wherein x is 2 to 20; R_e and R_f are each independently hydrogen, lower alkyl, cycloalkyl, aryl, heteroaryl, arylalkyl, amino, alkylamino, amido, alkylamido, dialkylamino, or carboxy; or R_e and

Pending Claims
US Application No. 09/478,222

R_f taken together are carbonyl, cycloalkyl or bridged cycloalkyl; and B is fluoro, C₁-C₆ alkoxy, cyano, carboxamido, cycloalkyl, arylalkoxy, alkylsulfinyl, arylthio, alkylamino, dialkylamino, hydroxy, carbamoyl, N-alkylcarbamoyl, N,N-dialkylcarbamoyl, amino, hydroxyl, carboxyl, hydrogen, nitro or aryl.

66. A method for treating human impotence in an individual in need thereof comprising administering to the individual a therapeutically effective amount of a composition comprising a NONOate and a pharmaceutically acceptable carrier.
67. The method of claim 66, wherein the human impotence is male impotence.
68. The method of claim 67, wherein the human impotence is female impotence.
69. The method of claim 66, wherein the composition is administered topically.